

CARCINOID TUMORS

Definition:

- neoplasm originating from neuroendocrine tissue found along the primitive GI tract
- neuroendocrine cells which perform amine uptake and decarboxylation (Kulchitsky cells), not derived from neural crest as previously thought

Epidemiology:

- incidence is 2 cases per 100,000 people
- much higher rate of clinically silent carcinoids: discovery at autopsy 1.2%
- often diagnosed in 5th decade
- higher incidence in African-Americans and women

Distribution:

- 74% of carcinoids arise in GI tract, distribution mirrors normal distribution of neuroendocrine cells

<i>Foregut</i>	
Esophagus	<1%
Stomach	2-30%
Duodenum	2-5%
Pancreas	<1%
Bronchopulmonary complex	10-25%

<i>Midgut</i>	
Jejunum	1-2%
Ileum	15-20%
Appendix	19-35%
Ascending colon	1-5%
Liver	<1%
Ovary	<1%

<i>Hindgut</i>	
Transverse Colon	1-5%
Descending colon	2-5%
Rectum	10-12%

Clinical presentation:

- 40-60% of patients are asymptomatic at presentation (coincidental appendicitis)
- carcinoid syndrome occurs when the various hormones produced by the tumor escape enteral hepatic circulation and metabolization (hepatic metastases, ovarian carcinoid)
- overall incidence of carcinoid syndrome 10-18%

<i>Symptoms of carcinoid syndrome</i>	<i>Frequency</i>
Flushing	<85-90%
Diarrhea	70%
Abdominal pain	35%
Bronchospasm	15%
Pellegra	5%
Heart disease	40%
Telangiectasia	25%

Etiology:

- as with most neoplasms, unclear inciting factors
- gastrin known to be tumorigenic: higher incidence of gastric carcinoid in patients with Zollinger-Ellison syndrome and chronic atrophic gastritis (both conditions with chronically elevated levels of gastrin)
- possible field effect:
- 28% of patients have multiple carcinoid primaries (*not* metastases),
- 17-53% have synchronous non-neuroendocrine cancer
- unclear association w/ MEN I (parathyroid, pancreatic, and pituitary tumors), largely pulmonary carcinoid seen in 10% of patients w/ MEN I

Diagnosis:

- 24 hour urinary 5-HIAA, 88% specificity
- normally, 99% of dietary tryptophan is metabolized into nicotinic acid, <1% made into 5-HTP. In carcinoid, ~60% is shunted to 5-HTP→5-HIAA.
- Level of 5-HIAA correlates with size of tumor
- plasma chromogranin A level, 80-100% sensitive, but not specific
- radiolabeled octreotide scan, 80-90% sensitivity

Treatment:

- symptomatic: avoiding stress and substances that precipitate flushing, dietary supplementation of niacin
- somatostatin receptor-targeted therapy inhibits release of growth hormone, gastrin, secretin, etc., also directly cytostatic to tumor cells. Octreotide found to increase survival duration
- chemotherapy not effective
- no cure for metastatic carcinoid

Resection:

- if <2cm, and no nodal invasion, local resection is curative
- resection of solitary liver metastasis beneficial
- vascular occlusion therapy: liver metastases largely supplied by hepatic artery, embolization may provide symptomatic relief in cases of carcinoid syndrome

Prognosis:

- tumor size is predictive of metastatic potential and prognosis
- presence of carcinoid syndrome is poor prognostic indicator, survival 3.5-8.5 years

Goblet cell variant

- rare variant, “adenocarcinoid”, mucin-filled
- displays both mucin production and neuroendocrine function because it arises from a pluripotent stem cell that differentiates into both cell lines
- appendiceal goblet cell carcinoids present as appendicitis
- more aggressive and unpredictable course, increased proliferation rate
- demands more aggressive resection, eg right hemicolectomy

- study of 9 patients: all had peritoneal metastases, 4 died w/in 2 years of diagnosis

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